REMARKS

Applicants and their Attorney would like to thank the Examiner for the courtesy of the telephonic interview of October 13, 2004 during which the foregoing claim amendments were discussed.

Claims 1-3, 11-12, 15-19, 24, 25 and 26 were pending in the application. Claims 1, 3, 17, 19, and 25 have been amended and claim 26 has been cancelled. Accordingly, after the amendments presented herein have been entered, claims 1-3, 11-12, 15-19, and 24-25 will remain pending. Support for the amendments to the claims may be found throughout the specification including the originally filed claims. Specifically support for the activity limitations recited in claims 1, 3, 17, 19 and 25 may be found, for example, at page 2, lines 34-35; page 10 lines 24-38; and in Example 10 at pages 49-52 of the specification.

No new matter has been added. Any amendments to the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and were done solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Indication of Certain Claims as Allowable

Applicants would like to thank the Examiner for the indication of claims 1-3 and 25 as allowable.

Withdrawal of Certain Rejections

Applicants would like to thank the Examiner for the withdrawal of the previous rejection of claims 1-3 and 25 under 35 U.S.C. 112, first paragraph as lacking enablement and written description.

Rejection of Claims 11-12, 15-19, 24 and 26 Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 11-12, 15-19, 24 and 26 under 35 U.S.C. 112, first paragraph because, according to the Examiner, the specification "while being enabling for a method of identifying a compound which binds to Kv4.2 or Kv4.3 and/or modulates the potassium channel activity of Kv4.2 or Kv4.3, does not reasonably provide enablement for a

method of identifying a compound which binds and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel, or a method of identifying a compound which binds and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel by contacting a biologically active PCIP polypeptide fragment." Specifically, the Examiner is of the opinion that

> [t]he rejection of record set forth that in the instant case, the claims are directed to a method of identifying a compound that binds and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel, or a method of identifying a compound that binds and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel by contacting a biologically active PCIP polypeptide fragment. Since the claims are directed to methods using biologically active fragments of PCIP 9q polypeptides, the claims encompass methods using variant proteins. Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible fragments of PCIP 9q.

Applicants respectfully traverse this rejection for the following reasons.

Claims 17 and 19, and claims depending therefrom, are directed to screening methods which use ***specific*** and ***defined*** fragments of PCIP polypeptides. Specifically, the claimed methods use polypeptide fragments comprising an EF domain, a Kv4.3 or Kv4.2 potassium channel α subunit binding domain, or a C-terminal core domain of a 9q PCIP polypeptide. Applicants' specification contains ample teachings demonstrating that these ***specific*** fragments are functionally important. For example, Applicants teach in Example 10 that a fragment of KChIP2 (a.k.a. 9q) denoted KChIP2Δ2–67 was produced to confirm that the C-terminal domain of this protein was sufficient to modulate Kv4 current density. The results in this example demonstrate that indeed a fragment of human 9q comprising amino acid residues 68-252 is capable of modulating Kv4 currents. Applicants' specification also teaches (in Example 10) that the C-terminal core domain of 9q

(containing the C-terminal 185 amino acid amino acid residues of human 9q) is sufficient to interact with and modulate the current density of Kv4.2 in a way that is indistinguishable from full length 9q. The specification further teaches that the PCIP molecules of the invention contain calcium binding domains, *i.e.*, EF domains. For Example, in Example 12 Applicants teach that PCIP molecules contain calcium binding domains and map these domains within the PCIP polypeptides in Figure 21. Applicants also disclose in Figure 41 the specific amino acid residues that are involved with calcium binding. Further, Applicants provide examples of a mutational analysis of EF domain residues in Example 10 to confirm that the residues that are described are in fact part of the EF domain.

In view of the fact that the rejected claims are directed to screening methods which use ***specific*** 9q PCIP polypeptide fragments that have been shown by Applicants to be functionally important, it would not require undue experimentation on the part of the skilled artisan to practice the claimed invention. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the foregoing rejection.

Rejection of Claims 11-12, 15-19, 24 and 26 Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 11-12, 15-19, 24 and 26 under 35 U.S.C. 112, first paragraph as "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record set forth in the Office Action of 10/30/2003" Specifically, the Examiner is of the opinion that

> [t]he rejection of record set forth that these are genus claims. The claims are drawn to a method of identifying a compound that binds and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel, or a method of identifying a compound that binds and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel by contacting a biologically active PCIP polypeptide fragment. Since the claims are directed to methods using biologically active fragments of PCIP 9q polypeptides, the claims encompass methods using variant proteins. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limit on the number of amino acid deletions that may be made to the PCIP 9q fragment. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claims do not provide any

guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus.

The Examiner also states that,

[t]he term "biologically active" is not defined by the claims, and no definition is given as to what this activity is. Various biological activities can be attributed to a peptide. For example, "activity" could constitute transportation throughout a cell, alteration of tertiary structure due to changes in pH, ligand binding, or modulation of second messenger effect, etc. 'Activity' could also be referring to the ability of the fragment to stimulate antibody production. Applicant argues that there is sufficient written description in the Specification regarding the specific fragments of PCIP 9q. However, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Applicants respectfully traverse this rejection.

As stated above, the instant claims are directed to screening methods which use ***specific*** and ***defined*** fragments of PCIP. Specifically, the claimed methods use polypeptide fragments comprising an EF domain, a Kv4.3 or Kv4.2 potassium channel α subunit binding domain, or a C-terminal core domain of a 9q PCIP polypeptide. As indicated above, Applicants' specification contains ample teachings demonstrating that these ***specific*** fragments are functionally important. For example, Applicants teach in Example 10 that a fragment of KChIP2 (a.k.a. 9q) denoted KChIP2Δ2–67 was produced to confirm that the C-terminal domain of this protein was sufficient to modulate Kv4 current density. The results in this example demonstrate that indeed a fragment of human 9q comprising amino acid residues 68-252 is capable of modulating Kv4 currents. Applicants' specification also teaches (in Example 10) that the C-terminal core domain of 9q (containing the C-terminal 185 amino acid amino acid residues of human 9q) is sufficient to interact with and modulate the current density of Kv4.2 in a way that is indistinguishable from full length 9q. The specification further teaches that the PCIP molecules of the invention contain calcium binding domains, *i.e.*, EF domains. For Example, in Example 12 Applicants teach that PCIP molecules contain calcium binding domains and map these domains within the PCIP

polypeptides in Figure 21. Applicants also disclose in Figure 41 the specific amino acid residues that are involved with calcium binding. Further, Applicants provide examples of a mutational analysis of EF domain residues in Example 10 to confirm that the residues that are described are in fact part of the EF domain.

Based on the foregoing teachings and the working examples in Applicants' specification, one of ordinary skill in the art would understand that Applicants were in possession of the claimed methods at the time the application was filed. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the foregoing rejection.

Rejection of Claims 11-12, 15-19, 24 and 26 Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 11-12, 15-19, 24 and 26 under 35 U.S.C. 112, first paragraph as, "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Specifically, the Examiner is of the opinion that

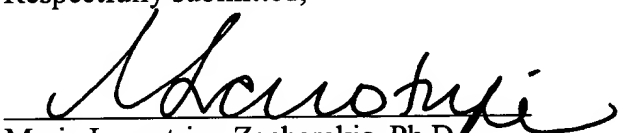
> [c]laims 17-19 are vague and indefinite in the recitation of the term "biologically active". The term "biologically active" is not defined by the claim, but give no definition of what this activity is. Various biological activities can be attributed to a peptide. For example, "activity" could constitute transportation throughout a cell, alteration of tertiary structure due to changes in pH, ligand binding, or modulation of second messenger effect, etc. 'Activity' could also be referring to the ability of the fragment to stimulate antibody production. Claims 11-12,15-16, 24, 26 are rejected insofar as they depend on the recitation of the term "biologically active".

While in no way acquiescing to the validity of the Examiner's rejection and solely in the interest of expediting prosecution, Applicants have amended the claims such that the term "biologically active" is no longer recited in the claims, thereby rendering this rejection moot. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the foregoing rejection.

CONCLUSION

Reconsideration and allowance of all the pending claims is respectfully requested. If a telephone conversation with Applicants' Attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

Respectfully submitted,



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Limited Recognition Under 37 C.F.R §11.9(b)

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